UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/665,455 | 09/18/2003 | Arlene A. Wise | S-100,654 | 6835 |

35068 7590 01/05/2007

LOS ALAMOS NATIONAL SECURITY, LLC
LOS ALAMOS NATIONAL LABORATORY
PPO. BOX 1663, LC/IP, MS A187
LOS ALAMOS, NM 87545

| EXAMINER | |
|---|---|
| RAMIREZ, DELIA M | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 01/05/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

TH

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/665,455 | WISE ET AL. | |
| | Examiner | Art Unit | |
| | Delia M. Ramirez | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *9-25* is/are pending in the application.

4a) Of the above claim(s) *13-20 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12,21 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *abstract-sousa et al.*.

## DETAILED ACTION

### *Status of the Application*

Claims 9-25 are pending.

Applicant's supplemental election without traverse of Group Ia, claims 9-12, 21, 25 drawn in part to a method of detecting a phenolic compound with a mutant labeled DmpR-B21 (SEQ ID NO: 3), in a communication filed 10/2/2006 is acknowledged.

As indicated in the Office action mailed on 7/3/2006, the requirement as it relates to Groups II-VIII, as set forth in the restriction requirement mailed on 3/15/2006, is deemed proper and therefore is made FINAL.

Claims 13-20, 22-24 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 9-12, 21 and 25 are at issue and are being examined herein.

### *Specification*

1. The specification is objected to for the following reasons. The amendment filed 9/18/2003 of the first paragraph of the specification does not contain the current status of U.S. Application No. 09/520538. Appropriate correction is required.

2. Applicant's request to amend the "Sequence Listing" by deleting SEQ ID NO: 8-13 from the "Sequence Listing" has not been entered for the following reasons. As set forth in 37 CFR 1.825(a)(b), any amendment to a paper copy of the "Sequence Listing" must be made by the submission of substitute sheets and include a statement that the substitute sheets include no new matter. In addition, any amendment to the paper copy of the "Sequence Listing," must be accompanied by a substitute copy of the computer readable form including all previously submitted data with the amendment incorporated therein. Applicant is reminded that if sequences are going to be deleted from the specification, a statement

indicating the reasons why such deletion would not constitute new matter may be required. Also, Applicant is reminded that the specification in its current form contains references to those sequences which Applicant intends to delete. Thus, amendments to the specification may be required to reflect those changes made to the Sequence Listing.

***Oath/Declaration***

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because the filing date of provisional application 60/123659 is incorrect. According to PTO records, the correct filing date is 3/9/1999.

***Priority***

4. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/123,659 filed on 03/09/1999.

5. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/520,538 filed on 03/08/2000.

***Drawings***

6. The drawings submitted on 9/18/2003 have been reviewed and are objected to for the following reasons. Figure 2b discloses a bar labeled 164 which does not correspond to either wild-type or DmpR-B21. The symbol for wild-type contains dots. The symbol for DmpR-B21 contains lines. The bar labeled 164 does not contain either dots or lines. The Examiner will assume that the bar labeled 164 has lines and corresponds to DmpR-B21. Appropriate correction is required.

***Claim Objections***

7. Claims 10 and 12 are objected to in view of the fact that they are partially directed to non-elected subject matter (i.e., DmpR-B23, DmpR-D9, DmpR-B17#2, DmpR-B9, and DmpR-D12). Appropriate correction is required.

8. Claim 25 is objected to due to the recitation of "culturing a bacteria". This should be amended to recite "culturing bacteria" since bacteria is the plural of bacterium. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 9-12, 21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 9, 11, 21, and 25 (claims 10 and 12 dependent thereon) are indefinite in the recitation of "DmpR" for the following reasons. As written, the term appears to be generic and not limited to a specific organism. While the gene nomenclature used may be appropriate for a transcriptional activator of the dimethylphenol (dmp) operon of *Pseudomonas* cells, the use of this nomenclature for proteins of identical function in other organisms may not be accurate. As known in the art, genes encoding proteins of identical function in two different organisms may use different designations. For example, the ARO4 gene of *Candida albicans* encodes a DAHP synthase whereas the *E. coli* counterpart is the aroF gene. See the abstract of Sousa et al. (Microbiology 148(Pt5):1291-1303, 2002). As such, the use of gene terminology which is applicable to some organisms and not to others is confusing since the claims use this nomenclature with respect to any organism. For examination purposes, the term "DmpR gene" will be interpreted "gene encoding a transcriptional activator of dimethylphenol catabolizing genes". If

Applicants wish to use the recited terminology in the claims, it is suggested that the claims be amended to clearly indicate the organism associated with the specific gene designation. Correction is required.

12. Claims 10 and 12 are indefinite in the recitation of "wherein the DmpR mutant is selected from the group consisting of DmpR-B21...." for the following reasons. While the specification discloses that the nucleotide sequence of the DmpR sensor domain labeled DmpR-B21 is SEQ ID NO: 3, as written, it is unclear as to whether the mutated DmpR gene is limited to the *Pseudomonas sp.* strain CF600 DmpR gene wherein the coding region of the sensor domain comprises SEQ ID NO: 3, or whether the mutated DmpR gene is any gene encoding a transcriptional activation of any dimethylphenol catabolizing gene wherein the region coding the sensor domain comprises SEQ ID NO: 3 (i.e., hybrid gene). For examination purposes, it will be assumed that the claims refer to the *Pseudomonas sp.* strain CF600 DmpR gene wherein the coding region of the sensor domain comprises SEQ ID NO: 3. Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 9, 11, 21 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9, 11, 21 and 25 are directed to a method for detecting phenol, 2-chlorophenol, 2,4-dichlorophenol, 2,4-dimethylphenol, 2-nitrophenol, 4-nitrophenol or 4-chloro-3-methylphenol with a *Pseudomonas* or *Escherichia coli* cell comprising (1) a reporter gene under the control of a promoter

inducible by a genus of transcriptional activators of any dimethylphenol catabolizing gene, and (2) a genus of genes encoding any transcriptional activator of a dimethylphenol catabolizing gene, wherein said gene is mutated in the region encoding the sensor domain of the transcriptional activator to enhance its transcriptional activation response to a phenolic compound. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, there is no structural limitation recited with regard to the members of the genus of transcriptional activators of any dimethylphenol catabolizing gene, or the genus of genes encoding said transcriptional activators. Furthermore, there is no limitation as to the structural modifications which would result in said transcriptional activators to have an enhanced transcriptional activation response to the phenolic compounds recited, or the structural modifications which would result in a specific level of enhancement of the transcriptional activation response. While the *Pseudomonas sp.*

strain CF600 DmpR protein is known in the art and disclosed in the specification, and the specification discloses a few mutations made to the sensor domain of the *Pseudomonas sp.* strain CF600 DmpR protein which would affect the transcriptional activation response to some phenolic compounds, the specification fails to disclose the structures of all the genes encoding transcriptional activators of any dimethylphenol catabolizing gene, or all the structural modifications (i.e., mutations) in the sensor domain of any transcriptional activator as recited which would result in enhancement of the response to the phenolic compounds recited. There is no indication or suggestion that the mutations disclosed with respect to the *Pseudomonas sp.* strain CF600 DmpR sensor domain when applied to any transcriptional activator of any dimethylphenol catabolizing gene would also have the effect of enhancing the response to the recited phenolic compounds. Even if it is assumed that this is the case, there is no information as to whether the enhancement would amount to the specific level recited in claim 25 for any transcriptional activator of any dimethylphenol catabolizing gene.

The claims encompasses a large genus of genes which are functionally and structurally unrelated. A sufficient written description of a genus of polynucleotides may be achieved by a recitation of a representative number of polynucleotides defined by their nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, there are no structural features recited for the genus of genes required by the claims. Furthermore, while one could argue that the disclosure of the structure of the *Pseudomonas sp.* strain CF600 DmpR gene and its corresponding protein provides adequate description for all the members of the genus, it is noted that the art teaches several examples of how even small changes in structure can lead to changes in function. For example, Witkowski et al. (Biochemistry 38:11643-11650, 1999) teach that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teach that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence

identity catalyze two different reactions: deamination and dehalogenation, therefore having different biological function. Therefore, since (a) minor structural changes may result in changes affecting function, (b) there is no additional information correlating structure with function, (c) there is no teaching or suggestion as to which are the structural elements in the gene disclosed in the specification that are required in any gene encoding a protein as required, and (d) no information has been provided with regard to additional mutations that would result in enhancement of the response to the recited phenols, one cannot reasonably conclude that the teachings of the specification and the prior art adequately describe the claimed method.

Due to the fact that the specification only discloses a single species of the genus of transcriptional activators of dimethylphenol catabolizing genes and a few mutations in the sensor domain of a single transcriptional activator, and the lack of description of any additional species by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

15. Claims 9, 11, 21 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting 2-chlorophenol and 2,4-dichlorophenol with a *Pseudomonas* or *Escherichia coli* cell comprising (a) a reporter gene under the control of a promoter inducible by the DmpR protein of *Pseudomonas sp.* strain CF600, and (b) a *Pseudomonas sp.* strain CF600 DmpR gene mutated such that the coding region of the sensor domain comprises SEQ ID NO: 3, does not reasonably provide enablement for a method for detecting phenol, 2-chlorophenol, 2,4-dichlorophenol, 2,4-dimethylphenol, 2-nitrophenol, 4-nitrophenol or 4-chloro-3-methylphenol with a *Pseudomonas* or *Escherichia coli* cell comprising (1) a reporter gene under the control of a promoter inducible by any transcriptional activator of any dimethylphenol catabolizing gene, and (2) a gene encoding any transcriptional activator of a dimethylphenol catabolizing gene, wherein said gene is

mutated in the region encoding the sensor domain of the transcriptional activator to enhance its transcriptional activation response to a phenolic compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims. The factors which have lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed in detail below.

***The breath of the claims***. Claims 9, 11, 21 and 25 are so broad as to encompass a method for detecting phenol, 2-chlorophenol, 2,4-dichlorophenol, 2,4-dimethylphenol, 2-nitrophenol, 4-nitrophenol or 4-chloro-3-methylphenol with a *Pseudomonas* or *Escherichia coli* cell comprising (1) a reporter gene under the control of a promoter inducible by a genus of transcriptional activators of any dimethylphenol catabolizing gene, and (2) a genus of genes encoding any transcriptional activator of a dimethylphenol catabolizing gene, wherein said gene is mutated in the region encoding the sensor domain of the transcriptional activator to enhance its transcriptional activation response to a phenolic compound. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation.

The enablement provided is not commensurate in scope with the claims due to the extremely large number of genes of unknown structure encoding a transcriptional activator of any dimethylphenol catabolizing gene as well as the potentially large number of unknown modifications encompassed by the claims. In the instant case, the specification enables a method for detecting 2-chlorophenol and 2,4-dichlorophenol with a *Pseudomonas* or *Escherichia coli* cell comprising (a) a reporter gene under the

control of a promoter inducible by the DmpR protein of *Pseudomonas sp.* strain CF600, and (b) a *Pseudomonas sp.* strain CF600 DmpR gene mutated such that the coding region of the sensor domain comprises SEQ ID NO: 3.

***The amount of direction or guidance presented and the existence of working examples.*** The specification discloses a mutated *Pseudomonas sp.* strain CF600 DmpR gene, wherein the mutations made to such gene are solely in the coding region of the sensor domain DmpR protein, and wherein the portion of the gene encoding the sensor domain comprises SEQ ID NO: 3, as a working example. However, the specification fails to disclose (1) the structures of all the genes encoding transcriptional activators of any dimethylphenol catabolizing gene, (2) all the structural modifications (i.e., mutations) in the sensor domain of any transcriptional activator as recited which would result in enhancement of the response to the phenolic compounds recited, (3) whether the mutations disclosed with respect to the *Pseudomonas sp.* strain CF600 DmpR sensor domain when applied to any transcriptional activator of any dimethylphenol catabolizing gene would also have the effect of enhancing the response to the recited phenolic compounds, or (4) whether the mutations disclosed when applied to any transcriptional activator of any dimethylphenol catabolizing gene would result in enhancement to the specific level recited in claim 25.

***The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art.*** The nucleotide sequence of the coding region of a polynucleotide determines the structural and functional properties of a protein encoded by that polynucleotide. Neither the specification nor the art provide a correlation between structure and activity such that one of skill in the art can envision the structure of any gene encoding a transcriptional activator of any dimethylphenol catabolizing gene. In addition, the prior art does not provide any teaching or guidance as to (1) which structural elements in the *Pseudomonas sp.* strain CF600 DmpR gene are essential for any gene to encode a transcriptional activator of any dimethylphenol catabolizing gene, (2) the structural modifications in the

sensor domain of any transcriptional activator of any dimethylphenol catabolizing gene which would result in an enhanced transcriptional activation response to the recited phenolic compounds, and (3) the modifications of (2) which would result in enhancement of such response to the specific level recited in claim 25.

While the argument can be made that the structure of the *Pseudomonas sp.* strain CF600 DmpR gene and the mutations disclosed in the specification enable the genus of genes required by the claimed invention, as one could use structural homology to isolate other genes encoding proteins of similar function and mutated them to enhance the transcriptional activation response to phenolic compounds, the art clearly teaches that structural changes in a protein to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide's sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247, 1991) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing *de novo* stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. and Seffernick et al. already discussed above, where it is shown that even small amino acid changes result in enzymatic activity changes.

***The quantity of experimentation required to practice the claimed invention based on the teachings of the specification.*** While methods of generating or isolating variants of a polynucleotide were known in the art at the time of the invention, it was not routine in the art to screen by a trial and error process for the extremely large number of polynucleotides encompassed by the claims. In the

absence of (1) some knowledge or guidance as to the structural elements required in any polynucleotide encoding the recited proteins, (2) a correlation between structure and function, and/or (3) some knowledge or guidance as to the structural modifications required in the sensor domain of any transcriptional activator of any dimethylphenol catabolizing gene, one of skill in the art would have to test an essentially infinite number of polynucleotides to determine which ones have the desired biological activity.

Therefore, taking into consideration the extremely broad scope of the claim, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and the desired function, and the high degree of unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

***Art of Interest***

16. Pavel et al. (J. Bacteriol. 176(24):7550-7557, 1994) discloses *P. putida* strains which comprise a reporter luciferase gene under the control of the *Pseudomonas sp.* strain CF600 dmp operon promoter Po, wherein said strains comprise a mutated *Pseudomonas sp.* strain CF600 DmpR gene, wherein the mutation is in the amino terminal A domain (sensor domain), and wherein said mutation confers the strains enhanced utilization and detection of 3-methylphenol, 4-methylphenol, 3,4-dimethylphenol, and 4-ethylphenol.

***Allowable Subject Matter***

17. A method for detecting 2-chlorophenol or 2,4-dichlorophenol in a test sample, wherein said method comprises the steps of (1) culturing a *Pseudomonas* or *Escherichia coli* cell comprising (a) a reporter gene under the control of the Po promoter inducible by the DmpR protein of *Pseudomonas sp.* strain CF600, and (b) a *Pseudomonas sp.* strain CF600 DmpR gene mutated at the coding region of the sensor domain, wherein the coding region of the sensor domain of the mutated *Pseudomonas sp.* strain CF600 DmpR gene comprises SEQ ID NO: 3, wherein said mutation results in enhanced transcriptional activation response to 2-chlorophenol and 2,4-dichlorophenol relative to the response obtained with wild type *Pseudomonas sp.* strain CF600 DmpR protein, and (2) detecting the expression of the reporter gene, wherein expression of the reporter gene is indicative of the presence of 2-chlorophenol or 2,4-dichlorophenol, appears to be allowable over the prior art of record.

***Conclusion***

18. No claim is in condition for allowance.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571)

272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
December 21, 2006